UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
ADDRESS: ASSISTANT COMMISSIONER FOR PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/734,613	12/13/2000	Marianne Bruggemann	37945-0009	3627

26633 7590 01/29/2003

HELLER EHRMAN WHITE & MCAULIFFE LLP
1666 K STREET,NW
SUITE 300
WASHINGTON, DC 20006

EXAMINER	
WEHBE, ANNE MARIE SABRINA	

ART UNIT	PAPER NUMBER
1632	15

DATE MAILED: 01/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/734,613	Bruggemann
Examiner	**Art Unit**
Anne Marie Wehbé	1632

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Oct 23, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above, claim(s) *14, 15, and 30-34* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-13 and 16-29* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☒ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's response to the restriction requirement received on 10/23/02 has been entered. Applicant's election with traverse of Group I, claims 1-13 and 16-29 is acknowledged. As applicants have not presented arguments in support of their traversal of the grounds for restriction, the restriction requirement is maintained for reasons of record as put forth in detail in paper no. 12. The requirement is still deemed proper and is therefore made FINAL. Claims 14-15 and 30-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 13. Claims 1-13 and 16-29 are currently under examination in the instant application. An action on the merits follows.

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Great Britain on 11/3/98. It is noted, however, that applicant has not filed a certified copy of the GB 9823930.4 application as required by 35 U.S.C. 119(b).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-13 and 16-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,162,963 (12/19/00), filed on 6/5/95, and hereafter referred to as Kucherlapati et al., in view of Mendez et al. (1997) Nat. Genet., Vol. 15, 146-156 and Popov et al. (1996) Gene, Vo. 177, 195-201. The applicant claims transgenic mice which comprise a YAC of about 410 kb which contains a 380 kb region of the human lambda light chain locus in germline configuration including V, J, and C lambda genes. The applicant further claims said mice wherein the endogenous murine heavy and/or light chain loci have been inactivated, and/or wherein the mice further comprise a YAC containing a region of the human heavy chain locus in germline configuration and/or a region of the human kappa light chain locus in germline configuration. In

addition, the applicant claims said mice wherein the human lambda light chain is expressed in amounts equal to that of the endogenous murine kappa chain, or wherein the transgenic human lambda and transgenic human kappa light chains are expressed in approximately equal amounts.

Kucherlapati et al. teaches methods of making transgenic mice which comprise various germline segments of the human Ig loci in order to produce mice capable of reproducing the normal human antibody repertoire in response to antigen (Kucherlapati, columns 3-4). In particular, Kucherlapati teaches that transgenic mice can be produced from murine embryonic stem cells modified to include YACs using spheroplast fusion techniques (Kucherlapati et al., columns 13-16). Specifically, Kucherlapati teaches that a number of different transgenic mice can be produced using their methods including mice which have one or both of the murine endogenous light chain and/or heavy chain loci inactivated by homologous recombination, and which further contain human immunoglobulin heavy chain and/or human light chain genes (Kucherlapati et al., columns 11-12). Kucherlapati et al. further teaches that the human light chain genes can be either human kappa light chain genes or human lambda light chain genes or both kappa and lambda light chain genes (Kucherlapati et al., column 11, lines 30-36). Kucherlapati et al. further teaches various human heavy chain and light chain YACs useful for making transgenic mice (Kucherlapati, columns 29-33). Finally, Kucherlapati et al. provides particular motivation for making a mouse with disrupted expression of both endogenous Ig heavy and light chain genes, and which comprises human heavy chain, kappa light chain, and lambda light chain loci by teaching that such a mouse, ".. would allow for the production of purely human antibody

molecules without the production of host of host/ human chimeric antibodies" (Kucherlapati et l., column 11, lines 30-36).

Mendez et al. supplements Kucherlapati et al. by teaching the production of Tsunamis I and Tsunamis II. Mendez et al. teaches transgenic mice which have disrupted endogenous Ig heavy chain and light chain loci, and which further have incorporated YACs comprising contiguous germline segments of the human Ig heavy chain and kappa light chain loci (Mendez et al., pages 146 and 154-155). In particular, Mendez et al. teaches that in mice with one allele of the smaller Ig YACs, an equal distribution of human kappa and murine lambda light chain gene expression was observed (Mendez et al., page 153, column 1). Mendez et al. also teaches that human antibody diversity and repertoire in the xenomice strains recapitulates that seen in humans (Mendez et al., pages 153-154). It is further noted that the human Ig heavy chain YAC utilized by Mendez includes Cμ, Cδ, and Cγ genes (Mendez et al., page 148).

While Kucherlapati et al. teaches transgenic mice comprising unrearranged germline segments of the human lambda light chain loci, neither Kucherlapati et al. nor Mendez et al. specifically teaches a YAC encoding germline segments of the human lambda light chain loci. Popov et al. supplements Kucherlapati et al. and Mendez et al. by teaching the construction of a 420 kp YAC which contains 380 kb of the unrearranged germline human Ig lambda light chain locus (Popov et al., page 195). Please note that the YAC described by Popov is the exact YAC used by applicants. Popov et al. further provides motivation for using the YAC to produce transgenic mice useful for structure-function studies of the human Ig lambda locus (Popov et al.,

page 200, column 2). Thus, based on the motivation provided by Kucherlapati to make transgenic mice comprising germline segments of the human Ig lambda light chain loci, and the motivation provided by Popov et al. to use a 420 kb YAC comprising 380 kb of the human lambda light chain loci to make transgenic mice, it would have been *prima facie* obvious to the skilled artisan to use the 420 kb YAC described by Popov in the methods of making transgenic mice taught by Kucherlapati et al.. Further, based on the successful use of the methods taught by Kucherlapati to produce human Ig transgenic mice as taught by Mendez et al., the skilled artisan would have had a reasonable expectation of success in using the YAC taught by Popov et al. to introduce human lambda light chain genes into the germline of a mouse.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 7-11, and 27-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites wherein , "..the proportion of the κ and λ light chains expressed by said human lambda genes..". Since the human lambda locus does not contain any κ light chain genes, this statement is confusing such that the metes and bounds of the claim cannot be determined.

Claims 7-11 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Claim 12, which depends on claim 7-11, includes all the steps necessary to actually produce the desired mouse. In particular, please note that the YAC in step (a) of claim 7 cannot be introduced into the murine embryonic stem cells in the absence of protoplast fusion, see the limitations of claim 10. Further, step (b) recites "deriving a transgenic mouse from the cells of step (a)". The term "deriving" is vague and indefinite and fails to constitute any actual method step which would lead to a transgenic mouse from a cell.

Claims 27-29 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The claims recite a transgenic mouse carrying human λ light chain genes wherein the expression of the λ locus genes is equal or greater than that of the endogenous or transgenic human κ locus. The transgenic mouse as described does not appear to contain human κ locus genes, as such it would appear that the claims as written are missing the essential element that the transgenic mouse also carries human κ light chain genes.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Mon-Fri from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The technology center fax number is (703) 308-4242, the examiner's direct fax number is (703) 746-7024.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER